

Single photon emission computed tomography imaging of cerebral blood flow, blood–brain barrier disruption, and apoptosis time course after focal cerebral ischemia in rats

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Abstract

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Cerebral ischemia is a leading cause of disability worldwide and no other effective therapy has been validated to date than intravenous thrombolysis. In this context, many preclinical models have been developed and recent advances in preclinical imaging represent promising tools. Thus, we proposed here to characterize *in vivo* time profiles of cerebral blood flow, blood–brain barrier disruption and apoptosis following a transient middle cerebral artery occlusion in rats using SPECT/CT imaging. Rats underwent a 1-h middle cerebral artery occlusion followed by reperfusion. Cerebral blood flow, blood–brain barrier disruption and apoptosis were evaluated by SPECT/CT imaging using respectively ^{99m}Tc-HMPAO, ^{99m}Tc-DTPA and the experimental ^{99m}Tc-Annexin V-128, up to 14 days after middle cerebral artery occlusion. Histological evaluation of apoptosis has been performed using TUNEL method to validate the ^{99m}Tc-Annexin V-128 uptake. ^{99m}Tc-HMPAO cerebral blood flow evaluation showed hypoperfusion during occlusion, partially restored on days 4 and 7 and sustained up to 14 days after middle cerebral artery occlusion. ^{99m}Tc-DTPA SPECT/CT showed a blood–brain barrier disruption starting on day 1 post-middle cerebral artery occlusion, peaking on day 2, with barrier integrity totally restored on day 7. ^{99m}Tc-Annexin V-128 SPECT/CT imaging showed significant positive correlation with TUNEL immunohistochemistry and allowed ischemic-induced apoptosis to be detected from day 2 to day 7, peaking on day 3 after middle cerebral artery occlusion. Using SPECT/CT imaging, we showed that after transient middle cerebral artery occlusion in rat there was a sustained decrease in cerebral blood flow followed by blood–brain barrier disruption preceding meanwhile apoptosis. Rodent SPECT/CT imaging of cerebral blood flow, blood–brain barrier disruption and apoptosis appears to be an efficient tool for evaluating neuroprotective drugs and regenerative therapies against cerebral ischemia and time-windows for therapeutic intervention.

Keywords

Stroke, MCAO, brain–blood barrier, cerebral blood flow, apoptosis, SPECT

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